IMPRIME PGG IMPROVES THE EFFICACY OF CARBOPLATIN, PACLITAXEL AND CETUXIMAB CHEMOIMMUNOTHERAPY OF ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC)

Michael Thomas MD, Parvis Sadjadi MD, Jens Kollmeier MD, Zhonglin Hoo MD, Mandla Bosi PhD, Mary Antonyan PhD, Myra Patchen PhD, Jamie Lowe, Michelle Gargano, Richard D. Huhn MD, Keith Gordon, Paulette Mathison, Folker Schneider MD* | Biothera, Inc., Eagan MN USA 55121

ABSTRACT

Objective: To determine if the addition of the chemimunotherapeutic agent Imprime PGG® (PGG) to the standard of care chemotherapy regimen of carboplatin, paclitaxel and cetuximab results in improved overall survival (OS) and safety in patients with advanced NSCLC, a multi-center, randomized, double blind placebo-controlled phase II trial was conducted.

Methods: The primary objective of this study was to evaluate the objective response rate (ORR) and time to progression (TTP) in the evaluable population. The secondary objectives were to measure OS, PFS, and safety. A total of 90 patients were randomized to receive PGG (N=60) or placebo (N=30) in addition to chemotherapy. The primary endpoint, ORR, was calculated using the RECIST criteria at 6 weeks of treatment. The Log-rank test was conducted to compare the OS data.

Results: In the evaluable population, the ORR was 37% (95% CI: 15%-61%) in the PGG group vs. 13% (95% CI: 3%-40%) in the control group (p=0.014). The median OS was 26% longer in the PGG group (9.8 months) vs. 7.8 months in the control group (p=0.009). The median PFS for the PGG group was 9.8 months vs. 5.3 months in the control group (p=0.017).

Conclusions: Imprime PGG® has a good safety profile and was well tolerated. The addition of Imprime PGG® to chemotherapy resulted in improved ORR, PFS, and OS compared to chemotherapy alone. Imprime PGG® was associated with a 29% improvement in median survival time (9.8 months vs. 7.8 months).

INTRODUCTION

Lung cancer is the leading cause of cancer mortality, responsible for an estimated 159,480 deaths in the United States in the year 2005. It is an important cause of death worldwide with group of various histological subtypes of carcinomas, of which 80% are of non-small cell histology (NSCLC). The 5-year survival rates for patients with squamous cell histology, 6 of 6 BM metastasis, was 48% in the entire Imprime group (p=0.048 vs. control) and 39% in the control group. The objective response rate (ORR) was calculated using the RECIST criteria at 6 weeks of treatment. The Log-rank test was conducted to compare the OS data. In the efficacy population comprised of all treated subjects who had evaluable baseline and post-baseline scans, median overall survival was 11.2 months in the primary group (N=90) vs. 7.8 months in the control group (N=30) (p=0.009). The median OS for the PGG group was 9.8 months vs. 7.8 months in the control group (p=0.009). The median PFS for the PGG group was 9.8 months vs. 5.3 months in the control group (p=0.017).

CONCLUSIONS

Improvements in OS and PFS were observed with Imprime PGG® in both squamous and non-squamous histology subpopulations. The addition of Imprime PGG® to chemotherapy resulted in improved ORR, PFS, and OS compared to chemotherapy alone. Imprime PGG® was associated with a 29% improvement in median survival time (9.8 months vs. 7.8 months).

METHODS

Key inclusion and exclusion criteria are shown in Table 1. Patients who had evaluable baseline and post-baseline scans, median overall survival was 11.2 months in the primary group (N=90) vs. 7.8 months in the control group (N=30) (p=0.009). The median OS for the PGG group was 9.8 months vs. 7.8 months in the control group (p=0.009). The median PFS for the PGG group was 9.8 months vs. 5.3 months in the control group (p=0.017).

TABLE 1: Inclusion and Exclusion Criteria

INCLUSION CRITERIA

- Life expectancy >3 months
- Histologically confirmed NSCLC of any stage and histology
- No prior chemotherapy treatment
- At least one measurable lesion
- ECOG performance status 0-2
- Hematologic criteria:
  - Hemoglobin ≥10 g/dL
  - Platelet count ≥100,000/mcL
  - White blood cell count ≥3,500/mcL
- Serum creatinine ≤1.5 x upper limit of normal
- Bilirubin ≤1.5 x upper limit of normal
- Total serum protein ≥3.5 g/dL

EXCLUSION CRITERIA

- Known second malignancy
- Concurrent investigational therapy or investigational therapy within 30 days prior to the first scheduled dosing day
- Previous organ or bone marrow transplant

RESULTS

The proportion of patients surviving over time in the Safety population is shown in Table 4. The graphical display of the Kaplan Meyer analysis of Imprime PGG® in the Primary Efficacy population is shown in the Figure 1. The ORR was calculated using the RECIST criteria at 6 weeks of treatment. The Log-rank test was conducted to compare the OS data. In the efficacy population comprised of all treated subjects who had evaluable baseline and post-baseline scans, median overall survival was 11.2 months in the primary group (N=90) vs. 7.8 months in the control group (N=30) (p=0.009). The median OS for the PGG group was 9.8 months vs. 7.8 months in the control group (p=0.009). The median PFS for the PGG group was 9.8 months vs. 5.3 months in the control group (p=0.017).

SUMMARY AND COMMENTS

The addition of Imprime PGG® in the placebo treatment resulted in a statistically significant difference in OS (p=0.009) and PFS (p=0.017) compared to placebo. These findings support the use of Imprime PGG® as an adjuvant to chemotherapy in the treatment of advanced NSCLC.

- Objective response rate: The primary endpoint of the study was statistically significant overall as well as in various subgroups.
- OS: The addition of Imprime PGG® to chemotherapy resulted in improved survival compared to chemotherapy alone.
- Safety: The addition of Imprime PGG® to chemotherapy was well tolerated.

CONCLUSIONS

Improvements in OS and PFS were observed with Imprime PGG® in both squamous and non-squamous histology subpopulations. The addition of Imprime PGG® to chemotherapy resulted in improved ORR, PFS, and OS compared to chemotherapy alone. Imprime PGG® was associated with a 29% improvement in median survival time (9.8 months vs. 7.8 months).

REFERENCES


1. A phase II study of 300 mg of Imprime PGG® (PGG) (biologically derived standardized PGG) was conducted to determine whether PGG would improve the activity of the chemotherapy regimen carboplatin, paclitaxel and cetuximab in patients with advanced NSCLC. The study was designed as a double-blind, placebo-controlled, randomized phase II study in which subjects received either Imprime PGG® (N=160) or placebo (N=160) in addition to chemotherapy. The primary endpoint was the ORR, calculated using the RECIST criteria at 6 weeks of treatment. The Log-rank test was conducted to compare the OS data. In the efficacy population comprised of all treated subjects who had evaluable baseline and post-baseline scans, median overall survival was 11.2 months in the primary group (N=90) vs. 7.8 months in the control group (N=30) (p=0.009). The median OS for the PGG group was 9.8 months vs. 7.8 months in the control group (p=0.009). The median PFS for the PGG group was 9.8 months vs. 5.3 months in the control group (p=0.017).